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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/520,360 | 01/05/2005 | Julie Kay Bush | X-14884 | 5540 |

25885 7590 11/30/2010

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| EXAMINER | |
|---|---|
| QAZI, SABIHA NAIM | |
| **ART UNIT** | **PAPER NUMBER** |
| 1628 | |

| NOTIFICATION DATE | DELIVERY MODE |
|---|---|
| 11/30/2010 | ELECTRONIC |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patents@lilly.com

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/520,360 | BUSH ET AL. | |
| | Examiner | Art Unit | |
| | Sabiha Qazi | 1628 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *04 August 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *2 and 15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/4/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**Non-Final Office Action**

Claims 2 and 15 are pending. Amendments are entered.

**Summary of this Office Action dated 9/05/2010**

1. Continued Examination under 37 CFR 1.14
2. 35 USC § 112(2) --Rejection
3. 35 USC § 103(a) --Rejection
4. Response to Remarks
5. Communication

**Continued Examination Under 37 CFR 1.114**

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on –has been entered.

***Claim Rejections - 35 USC § 112***

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1 and 15 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Following reasons apply:

3. Claim should start from “A”. The “C” of Crystalline should be in lower case. The amendment is suggested.

**Claim Rejections - 35 USC § 103**

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor

and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2 and 15 are rejected under 35 USC § 103(a) as being obvious over DHINGRA, U,[1] TEICHER et al[2], HEATH et al.

DHINGRA teaches the compounds and hydrochloride salts of the claimed compound. The reference teaches crystallized mono hydrochloride salts of such and similar compounds and method for making them. See example 7 on page 31. The reference teaches "The conversion of an acidic compound of formula 1 into a pharmaceutically acceptable salt can be carried out by treatment with a suitable base in a known manner. Suitable bases are those derived not only from inorganic bases, for example, sodium, potassium or calcium salts, but also from organic bases such as ethylenediamine, monoethanolamine or diethanolamine. The conversion of a basic compound of formula I into a acceptable salt can be carried

[1] URVASHI DHINGRA, WO 98/04551, see the entire document especially lines 32-35, page 12, lines 1-35 on page 13, compound of formula (I), abstract and claims.

out by treatment with a suitable acid in a known manner. Suitable salts are those derived not only from inorganic acids, for example, hydrochlorides, hydrobromides, phosphates or sulphates, but also from organic acids, for example, acetates, citrates, fumaratess, tartarates, maleates, methanesulphonates or p-toluenesulphonates. The pyrroles of formula I and their pharmaceutically acceptable salts inhibit cellular processes, for example cell proliferation, and can be used in the treatment or control of inflammatory disorders such as arthritis, immune diseases, in conjunction with organ transplants and in oncology", Lines 1-13 on page 13.

TEICHER et al discloses 3-[l- (1-(pyridin-2 methyl) piperidin-4-yl)-indol-3-yl]-4-(1 -methyhndol-3-yl)- 1H-pyrrole-2,5-dione (FB) or a pharmaceutically acceptable salt or solvate thereof (see lines 1-10 on page 7). It further teaches, "Because it contains a basic moiety, the compound of Formula I can also exist as pharmaceutically acceptable acid addition salts. Acids commonly employed to form such salts include inorganic acids such as **hydrochloric acid** (lines 13-32,

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[2] BEVERLY TEICHER et al; World Intellectual Property Organization Publication Number WO 02/02094 A2, published January 10, 2002. See the entire document, especially lines 6-10 on page 9, lines 1-10 on page 7, lines 27-30 on page 11, all of pages 12-20, examples, 49and claims.

page 8). Reference further teaches that the pharmaceutically acceptable salts of the compound of Formula I can also exist as **various solvates, such as with water**, methanol, ethanol, dimethylformamide, ethyl acetate and the like. **Mixtures of such solvates can also be prepared**. The source of such solvate can be from the **solvent of crystallization, inherent in the solvent of preparation or crystallization, or adventitious to such solvent.** See lines 29-32, page 8. The reference further teaches that particularly hydrochloride and mesylate salts are used, see line 27 and 28, page 8).

HEATH et al discloses 3-[l- (1-(pyridin-2 methyl)piperidin-4-yl)-indol-3-yl]-4-(1 -methyhndol-3-yl)- 1H-pyrrole-2,5-dione (FB). See example 49 in column 45 where the compound is disclosed. This compound is a protein kinase inhibitor. The reference teaches pharmaceutically acceptable salts such as hydrochloric salts.[3] See the entire document especially lines 37-67 in column 10; lines 1-12 in column 11. The reference also teaches the compounds are potent, beta-1 and beta-2 isozyme selective PKC inhibitors.

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[5] WILLIAM F. HEATH, JR. et al; United States Patent No. 5,545,636, published August 13 1996. See the entire document especially example 49 in columns 45 and 46, formulas II and III in column 3 and 4, lines 37-67 in col. 10; lines 1-4 in column 11.

X-diffarction, H-NMR, $C^{13}$ NMR are the tools in analytical chemistry, very commonly used to determine structure of compounds. At the time the invention was filed X-ray diffraction was available and does not give wait to patentability of the compound for being a monohydrochloride.

Instant claims differ from the reference in claiming the composition and citing X-diffraction peaks.

It would have been obvious to one skilled in the art at the time of invention was made to prepare the crystalline pharmaceutically acceptable salts such as monohydrochloride salts of known compound because the prior art DHINGRA teaches the crystallized monohydrocholrides TEICHER et al and HEATH teaches the crystalline forms of dihydrochloride and teaches that since it contains a basic moiety, it can also exist as pharmaceutically acceptable acid addition salts. Acids commonly employed to form such salts include inorganic acids such as hydrochloric acid (lines 13-32, page 8), so the monochloride salt would be fairly suggested thereby.

In the light of the forgoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined by the instant claims would have been obvious within the meaning of 35 U.S.C. 103(a).

**Communication**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sabiha Qazi whose telephone number is (571) 272-0622. The examiner can normally be reached on any business day except Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Fetterolf Brandon can be reached on (571) 272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sabiha Qazi/
Primary Examiner, Art Unit 1628